BMC Anesthesiology

ORAL PRESENTATION Open Access

Role of sarcoplasmic reticulum junctional proteins in skeletal muscle strength

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From 33rd Annual Meeting of the European Malignant Hyperthermia Group (EMHG)
Würzburg, Germany. 15-17 May 2014

Background

Skeletal muscle constitutes approximately 40% of body mass, and age-induced decrease of muscle strength impinge on daily activities and on normal social life in the elderly. Loss of muscle strength has been recognised as a debilitating and life threatening condition also in cachexia in cancer patients and in clinical conditions associated with prolonged bed rest. Skeletal muscle dihydropyridine receptors (Cav1.1) act as Ca2+ channels and voltage sensors to initiate muscle contraction by activating ryanodine receptors, the Ca2+ release channels of the sarcoplasmic reticulum. Cav1.1 activity is enhanced by a retrograde stimulatory signal delivered by the ryanodine receptor. JP45 is a membrane protein interacting with Cav1.1 and the sarcoplasmic reticulum Ca2+ storage protein calsequestrin (CASQ1).

We hypothesized that JP45 and CASQ1 form a signalling pathway which modulates Cav1.1 channel activity.

Materials and methods

We isolated flexor digitorum brevis (FDB) muscle fibres from JP45 and CASQ1 double knock-out mice (DKO) and tested whether there were differences in Ca2+ homeostasis between the different mouse lines.

Results

Our results show that Ca2+ transients evoked by tetanic stimulation in DKO fibres, result from massive Ca2+ influx due to enhanced Cav1.1 channel activity. This enhanced activity causes an increase of muscle strength both *in vitro* and *in vivo*.

Conclusions

We conclude that skeletal muscle contraction is strengthened through the modulation of Cav1.1 channel activity by JP45 and CASQ1.

Acknowledgements

This work was supported by funds from Swiss Muscle foundation, A.F.M., S.N. F and Department of Biomedicine University Hospital Basel. This study was also supported by Research Grant no. GGP08153 from the Italian Telethon ONLUS Foundation to F.P. and grants from the NIH/NIA (AG13934 and AG15820) to O.D.

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Published: 18 August 2014

doi:10.1186/1471-2253-14-S1-A19
Cite this article as: Mosca *et al.*: Role of sarcoplasmic reticulum junctional proteins in skeletal muscle strength. *BMC Anesthesiology* 2014 **14**(Suppl 1):A19.

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